Menkes syndrome

Menkes syndrome is a disorder that affects copper levels in the body. It is characterized by sparse, kinky hair; failure to gain weight and grow at the expected rate (failure to thrive); and deterioration of the nervous system. Additional signs and symptoms include weak muscle tone (hypotonia), sagging facial features, seizures, developmental delay, and intellectual disability. Children with Menkes syndrome typically begin to develop symptoms during infancy and often do not live past age 3. Early treatment with copper may improve the prognosis in some affected individuals. In rare cases, symptoms begin later in childhood.

Occipital horn syndrome (sometimes called X-linked cutis laxa) is a less severe form of Menkes syndrome that begins in early to middle childhood. It is characterized by wedge-shaped calcium deposits in a bone at the base of the skull (the occipital bone), coarse hair, and loose skin and joints.

Frequency

The incidence of Menkes syndrome and occipital horn syndrome is estimated to be 1 in 100,000 newborns.

Genetic Changes

Mutations in the *ATP7A* gene cause Menkes syndrome. The *ATP7A* gene provides instructions for making a protein that is important for regulating copper levels in the body. Copper is necessary for many cellular functions, but it is toxic when present in excessive amounts. Mutations in the *ATP7A* gene result in poor distribution of copper to the body's cells. Copper accumulates in some tissues, such as the small intestine and kidneys, while the brain and other tissues have unusually low levels of copper. The decreased supply of copper can reduce the activity of numerous copper-containing enzymes that are necessary for the structure and function of bone, skin, hair, blood vessels, and the nervous system. The signs and symptoms of Menkes syndrome and occipital horn syndrome are caused by the reduced activity of these copper-containing enzymes.

Inheritance Pattern

Menkes syndrome is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the

disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In about one-third of cases, Menkes syndrome is caused by new mutations in the *ATP7A* gene. People with a new mutation do not have a history of the disorder in their family.

Other Names for This Condition

- Copper transport disease
- Hypocupremia, Congenital
- Kinky Hair Syndrome
- Menkea syndrome
- Menkes Disease
- MK
- MNK
- Steely Hair Syndrome
- X-linked copper deficiency

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Menkes kinky-hair syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0022716/

Other Diagnosis and Management Resources

- GeneReview: ATP7A-Related Copper Transport Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1413
- MedlinePlus Encyclopedia: Copper in diet
  https://medlineplus.gov/ency/article/002419.htm
- MedlinePlus Encyclopedia: Menkes syndrome
  https://medlineplus.gov/ency/article/001160.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html

- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Copper in diet
  https://medlineplus.gov/ency/article/002419.htm
- Encyclopedia: Menkes syndrome
  https://medlineplus.gov/ency/article/001160.htm
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html

Genetic and Rare Diseases Information Center

- Menkes disease
  https://rarediseases.info.nih.gov/diseases/1521/menkes-disease

Additional NIH Resources

- Menkes Disease and Occipital Horn Syndrome International Registry
  https://menkesohs.nichd.nih.gov/
- National Institute of Neurological Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Menkes-Disease-Information-Page
- NIH News: NIH Scientists Detect Fatal Copper Disorder at Birth
  https://www.nih.gov/news-events/news-releases/nih-scientists-detect-fatal-copper-disorder-birth

Educational Resources

- Disease InfoSearch: Menkes disease
  http://www.diseaseinfosearch.org/Menkes+disease/4603
- MalaCards: menkes disease
  http://www.malacards.org/card/menkes_disease

- My46 Trait Profile
  https://www.my46.org/trait-document?trait=Menkes%20syndrome&type=profile
- Orphanet: Menkes disease
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=565

Patient Support and Advocacy Resources

- CLIMB: Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk
- National Organization for Rare Disorders
  https://rarediseases.org/rare-diseases/menkes-disease/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/menkes.html

GeneReviews

- ATP7A-Related Copper Transport Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1413

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22menkes+syndrome%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Menkes+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3240+days%22%5Bdp%5D

OMIM

- MENKES DISEASE
  http://omim.org/entry/309400
- OCCIPITAL HORN SYNDROME
  http://omim.org/entry/304150

Sources for This Summary

- Barnes N, Tsivkovskii R, Tsivkovskaia N, Lutsenko S. The copper-transporting ATPases, menkes and wilson disease proteins, have distinct roles in adult and developing cerebellum. J Biol Chem. 2005 Mar 11;280(10):9640-5. Epub 2005 Jan 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15634671
- Bertini I, Rosato A. Menkes disease. Cell Mol Life Sci. 2008 Jan;65(1):89-91. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17989919

- Donsante A, Tang J, Godwin SC, Holmes CS, Goldstein DS, Bassuk A, Kaler SG. Differences in ATP7A gene expression underlie intrafamilial variability in Menkes disease/occipital horn syndrome. J Med Genet. 2007 Aug;44(8):492-7. Epub 2007 May 11. Erratum in: J Med Genet. 2008 Jan;45(1): 64.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17496194
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2597922/
- GeneReview: ATP7A-Related Copper Transport Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1413
- Harris ED. Basic and clinical aspects of copper. Crit Rev Clin Lab Sci. 2003 Oct;40(5):547-86. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14653357
- Kaler SG, Holmes CS, Goldstein DS, Tang J, Godwin SC, Donsante A, Liew CJ, Sato S, Patronas N. Neonatal diagnosis and treatment of Menkes disease. N Engl J Med. 2008 Feb 7;358(6):605-14. doi: 10.1056/NEJMoa070613.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18256395
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3477514/
- Madsen E, Gitlin JD. Copper deficiency. Curr Opin Gastroenterol. 2007 Mar;23(2):187-92. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17268249
- Menkes JH. Menkes disease and Wilson disease: two sides of the same copper coin. Part I: Menkes disease. Eur J Paediatr Neurol. 1999;3(4):147-58. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10476363
- National Institute of Neurological Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Menkes-Disease-Information-Page
- Prohaska JR. Role of copper transporters in copper homeostasis. Am J Clin Nutr. 2008 Sep;88(3): 826S-9S.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18779302
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2799992/
- Tang J, Robertson S, Lem KE, Godwin SC, Kaler SG. Functional copper transport explains neurologic sparing in occipital horn syndrome. Genet Med. 2006 Nov;8(11):711-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17108763
- Voskoboinik I, Camakaris J. Menkes copper-translocating P-type ATPase (ATP7A): biochemical and cell biology properties, and role in Menkes disease. J Bioenerg Biomembr. 2002 Oct;34(5): 363-71. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12539963
- de Bie P, Muller P, Wijmenga C, Klomp LW. Molecular pathogenesis of Wilson and Menkes disease: correlation of mutations with molecular defects and disease phenotypes. J Med Genet. 2007 Nov;44(11):673-88. Epub 2007 Aug 23. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17717039
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2752173/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/menkes-syndrome

Reviewed: March 2009
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services